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KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
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ning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR TREATING, PREVENTING, OR REDUCING CARDIAC DISORDERS USING FADD
INHIBITORS

(57) Abstract: The present invention relates to methods for treating or preventing cardiac disorders such as heart failure, by adminis-
tering to a mammal a therapeutically effective amount of an FADD inhibitor. According to the present invention, the FADD inhibitor
is anti-apoptotic, anti-inflammatory, or both. Also disclosed are screening methods that make use of FADD for the identification of
novel therapeutics for treating or preventing cardiac disorders.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36624

| A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A01N 63/00; A61K 48/00; C12Q 1/00; C12N 15/00,09,63,70,74,85,86,87 US CL : 424/93.2,93.21; 435/4,320.1,455,456 According to International Patent Classification (IPC) or to both national classification and IPC | | |
|---|--|--|
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 424/93.2,93.21;435/4,320.1,455,456 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X — Y | CHAO et al. Role of FADD in hypoxia- and serum deprivation-induced cardiomyocyte apoptosis, page 293. | 33, 34, 38, 39, 56-64 ----- 29, 30, 35, 40 |
| X | CHAO et al. Importance of FADD signaling in serum deprivation- and hypoxia-induced cardiomyocyte apoptosis The Journal of Biological Chemistry. 30 August 2002, Vol 277, No. 35, pages 31639-31645. | 1, 4, 14, 16, 17, 19, 31-34, 36-39, 41, 43- 45, 47, 49, 50, 52-54, 56-64 ----- 2, 6, 7, 9, 10, 11, 12, 13, 21, 27-30, 35, 40 |
| X | SRINIVASula et al FLAME-1, a novel FADD-like anti-apoptotic molecule that regulates fas/TNFR1-induced apoptosis The Journal of Biological Chemistry. 25 July 1997, Vol 272, No. 30, pages 18542-18545. | 1, 4, 14, 16, , 17, 56- 64 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| * Special categories of cited documents: | | |
| "A" | document defining the general state of the art which is not considered to be of particular relevance | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
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| "O" | document referring to an oral disclosure, use, exhibition or other means | "A" document member of the same patent family |
| "P" | document published prior to the international filing date but later than the priority date claimed | |
| Date of the actual completion of the international search 14 May 2004 (14.05.2004) | | Date of mailing of the international search report 02 JUL 2004 |
| Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | | Authorized officer Brian Whiteman <i>Janice Ford</i> Telephone No. (703) 308-0196 <i>for</i> |

INTERNATIONAL SEARCH REPORT

PCT/US03/36624

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-------------|---|--|
| X — Y | US 6,242,569 B1 (SHU et al) 05 June 2001 (05.06.2001), see whole document, especially columns 2-6. | 56-64 1, 2, 14, 16, 17, 21, 22, 25, 26, 27, 31, 35, 36, 40-45, 47, 55 |
| X,P | US 6,605,426 B1 (GOLDBAKHER et al) 12 August 2003 (12.08.2003), see whole document, especially columns 20-32. | 1-6 and 8-64 |
| A | BOWEN-POPE et al Apoptosis of smooth muscle cells is not silent: Fas/FADD initiates a program of inflammatory gene expression TCM 2001, Vol 11, No. 1, pages 42-45. | 1-21 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/36624

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 7
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claim 7 depends on itself.
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

Continuation of B. FIELDS SEARCHED Item 3:

WEST2.1, STN

search terms: FADD, anti-apoptotic, anti-inflammatory, cardiomyocytes, heart, cardiac, dominant negative, inhibitor, vector, assay, screening